HYDROGEN EXCHANGE IN SOLUTIONS

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by A. I. Brodskiy

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It is well known that the additive properties of
parameters which characterize atoms and bonds approximate
the physical properties of molecules but are completely in-
adequate to explain their chemical behavior. This aspect
is not usually considered in studies of exchange reactions,
although these represent particular cases of common chemical
reactions. Even recently it was commonly considered that
capacity for hydrogen exchange and the rate of exchange de-
pend first of all on the nature of atom X in the X-H bond
where the exchange takes place. However, it is impossible
to find even one qualitative bond characteristic that would
explain the great differences in the rate of hydrogen ex-
change that are observed in the same medium under the same
experimental conditions. Moreover, as shown by the many
examples listed below, in such bonds as N-H or P-H the ex-
change proceeds immeasurably fast in some molecules and does
not proceed at all in others. Inductive and quantum-mech-
anical mutual interactions, which greatly influence the
speed of reaction, are clearly insufficient to explain these
differences in behavior.

Earlier (1) it was shown that the most realistic indi-
cations characterizing hydrogen exchange are the differences
in the structures of the electronic clouds around the atoms
to which the exchanging atoms of hydrogen are connected. By
this criterion hydrogen exchange reactions may be classified
into two basic types, depending on the mechanism* which de-
termines them, as shown in the papers (2) where the idea is
studied in greater detail. As will be shown later, these
ideas not only explain the characteristics of hydrogen

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*In this work radical mechanisms of exchange reactions in
solutions are not discussed, because the lack of experiment-
al data on such mechanisms prevents general conclusions from
being drawn.

exchange, but they can be successfully applied in predicting new facts in matter, and in some cases -- in the study of molecular structure.

Dependence of the Exchange upon the Structure of Electronic Clouds

The exchange in systems XH-YD, where YD, a donor of deuterium*, passes through an intermediate complex formed by the hydrogen bonds**, belongs to two qualitatively different types, depending upon the presence or absence of free (unsplit) electron pairs near the atoms X and Y. In the first case the exchange goes through complex (A) by the synchronized transition of H and D to free pairs***. Such a transition does not require a large activation energy since the free valencies already possess this energy, and the exchange takes place very rapidly. This kind of exchange is called fast.

(A)   X ———— H   (B)   X — — — H

     D   Y   D———— Y

$D^- \longrightarrow\ :X:H \longrightarrow$ $D^+\quad X:H \longrightarrow$
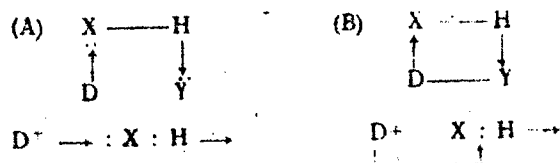
In the absence of free electron pairs near the atoms $\overline{X}$ or $\overline{Y}$ (or both) the transfer of H and D to complex (B) is possible only in pairs which first form bonds $\overline{X}$ - H and $\overline{Y}$ - D after they are completely or partly freed. These preliminary states require, as a rule, considerable activation energy, and the exchange either does not start at all or is more or less retarded. This type of exchange is called slow.

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*Atoms X and Y may be components of more complex molecules.
**N. D. Sokolov (27) demonstrated the part played by free electron pairs in forming hydrogen bonds.
***The quaternary complex is used only for the sake of simplicity. Considerations of its different structure can be found in the articles of Ya. K. Syrkin and N. D. Sokolov in this issue of the journal, and also in ref. (6). In this connection we must note that N. D. Sokolov protests unjustifiably against the assertions we develop here, basing his protest on the disadvantages of the quaternary complex from the energy point of view, he refers to an example which is not present in this work.

The exchange of the fast type always proceeds rapidly irrespective of the structural nature of the exchanging molecules, their acidity, or the properties of the medium. It requires no catalysts and is hardly sensitive to them. An exchange of this type reaches equilibrium before its kinetics can be measured by ordinary means (seconds and minutes). Such an exchange is referred to in the literature as "immeasurably fast."*

Conversely, the exchange of the second type may occur quickly only in exceptional cases of strong acid-base catalysis at a high temperature or with the introduction of highly activating groups; but it always proceeds slowly, or not at all, if such conditions are not present. For example, hydrocarbons exchange the hydrogen in C-H bonds very slowly with D_2O, but in some the exchange proceeds very fast in the very basic medium ND_3 in the presence of the very strong alkaline catalyst KND_2 (3). In contrast, the exchange of OH groups in any compound proceeds immeasurably rapidly in all media with such wide gradation of acidity as DBr, D_2SO_4, D_2O and ND_3.

Thus, the basic, experimentally observable indication of whether an exchange belongs to the first or second type is not its rate of exchange, but the dependence of the latter on structure and experimental conditions, as already noted (2).

Experimental Basis

Considerable experimental data are not available which confirm the ideas discussed here. In addition to those which we cited in former articles we may dwell on some new ones published in 1953-1954, by American authors, where our data are confirmed and new proof is obtained for the correctness of our views.

1. With the exception of two cases discussed below, not a single example is known where the exchange did not

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*It is to be regretted that more refined methods were not used for the kinetic study. They, no doubt, would have revealed the dependence of the rate upon the structure and medium, and would have justified more reliable conclusions about the mechanism of exchange. However, differences in rates in this type of exchange cannot be very great, since they, evidently, stay within limits of exchange in each stress (discounting diffusion) within seconds.

proceed "immeasurably fast" (in the foregoing sense) in the presence of free electron pairs.

Besides a multitude of well-known data on the exchange in the bonds O-H, N-H (ammonium, amino, imino) B-H, Cl-H and others (4) with D_2O let us consider new works. Hine ans Thomas (5) found that the exchange in bonds of O-H and N-H between water and ethyl alcohol (at 0°), between tributyl and n-heptylalcohols, or ethylamine (at -11°), reaches equilibrium quicker than it is possible to take samples for analysis (a few seconds). They explained the very fast exchange in these systems by our mechanism of the transition between H and D with the free pairs in the molecular complex (A). Kwart and co-workers (6) also found that in O-H bonds the exchange of H_2O and CH_3OH with D_2O or HDO also goes immeasurably fast (half-life of less than 20 sec.) and they explained it with similar molecular mechanisms without ionization. In contra-diction with these data V. V. Voyevodsky, G. K. Lavrovskaya, and R. D. Mardaleyshvily (7) have found indirectly (by sub-stitutions on a calibrated curve of heat conduction by steam) that the reaction $H_2O + D_2O = 2HDO$ proceeds very slowly in the liquid phase and is strongly catalyzed by salts. This contradiction remains unresolved and requires further experi-mental study. The slow exchange in the system $H_2O + D_2O$ with an immeasurably fast exchange in the system ROH + D_2O or $R_1OH + R_2OD$, if confirmed, will prove to be an exception of similar difficulty to any of the existing theories of hydrogen exchange.

The second exception refers to the exchange of phosphine with D_2O which, according to Weston and Bigeleisen (8), has measurable kinetics (energy of activation 17.6 kcal/mole) which is evidently not determined by the diffusion retardation of the PH_3 solution, and is noticeably catalyzed by acids and bases. It would be more correct to view this as yet only reliable exception to our thesis not as a refutation, but as a sign of the presence of associated processes which block the free electron pair in a solution of phosphorus. This reduces its capacity for hydrogen exchange and it moves, as the authors suppose, to the ions of $PH_4 +$ or $PH_2 -$ that are in equilibrium with PH_3. The state of PH_3 in solution is not well known, but such blocking of electron pairs by coor-dination with water and its ions may be assumed by analogy, for example, with well-known oxyhalide compounds of the type

$Cl_3P \rightarrow O$.*
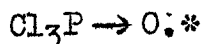
2. In the absence of free electron pairs, the exchange always shows the above-mentioned signs of the slow type.
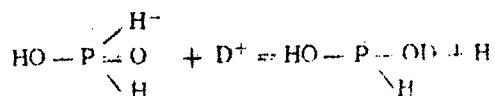
First of all we must mention the host of thoroughly investigated examples of exchange in the C-H bonds of organic compounds. This is observed only in the presence of groups which strongly polarize this bond, or in such very acid or very basic media as DF, DBr, D_2SO_4, ND_3. These conditions exert a determining effect on the speed of exchange.

The exchange in N-H bonds gives a visible confirmation of our assertions. It proceeds immeasurably fast in ammonia (10), amines, amino acids, and imines(11), where there is a free electron pair near the nitrogen atom. On the other hand, it is slowed down greatly if the pair is blocked. A slow exchange was discovered in the $-NH_3$ group of a series of amino compounds (12), also in the NH_4^+ ion of ammonium salts, as found by L. V. Sulima and the author (13). In the latter work it was shown that the exchange proceeds fully or basically not in this ion but in the free NH_3, which stays in hydrolytic equilibrium with it. Our results were confirmed and applied to salts of substituted ammonium by Kaplan and Wilzbach (14). They found a greatly retarded hydrogen exchange to tritium between C_2H_5OT and substituted ammonium salts, while in the N-H bonds of guanidine nitrate, which have free electron pairs, the exchange with alcohol occurs extremely fast. Further confirmation was obtained by Swain and co-workers (15). For an exchange in a series of substituted ammonium salts with CH_3OD they found a half-life of 2 to 200 minutes. These authors also assume that the exchange takes place in the displaced amine which results from the solvolysis of the substituted ammonium ion.

Investigations by I. G. Haskin and the author confirmed the expected great retardation of the exchange in Si-H bonds of trisilanes R_3Si-H, which does not proceed at all under severe conditions with D_2O, C_2H_5OD and $(C_2H_5)_2ND$. L. V. Sulima and the author (17) found in the P-H bonds of hypophosphites, phosphites, and H_3PO_3 no exchange with D_2O. In

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*Such a retardation of electron pairs in the formation of polysulfide chains may be the reason for the measurable kinetics of exchange $D_2S + C_2H_5OH$ found at low temperatures in earlier works (9). However, to explain this case, it is enough to accept the evaluation of the given activation energy of the fast exchange at which the exchange should be very fast at room temperature, and should slow down at -80°.

these compounds the phosphorus is in the P^V condition, in which there are no free electron pairs. Conversely, in phosphorous acid the exchange proceeds at a moderate rate, which is explained by tautomeric conversion into the P^{III} form with a free pair:

$$HO - P \underset{\underset{\displaystyle H}{\diagdown}}{\overset{\overset{\displaystyle H}{\diagup}}{=}} O \quad + \ D^+ \rightleftarrows HO - P - OD + H$$
$$\diagdown H$$

The exchange may take place at the moment of conversion (see scheme) as well as in the tautomer P^{III}. This supposition was finally confirmed by kinetic measurements and comparison with the kinetics of H_3PO_2 oxidation. Simultaneously and independently from us, Jenkins and Yost (18) came to the same conclusions upon studying the exchange of H_3PO_2 with HTO. Such tautomerism is absent in phosphorous acid and in the salts of both acids, as shown by a lack of hydrogen exchange in them. In H_3PO_3 tautomeric conversion is made more difficult by the presence of a second OH group, which increases the nucleophilic character of the P atom; this makes it more difficult to break the P-H bond, and in anions, evidently, - the combination of D^+ (or H^+) with the free charge of $P-O^-$ leads to the reconstruction of the acid with P^V, and prevents the exchange in the P-H bond.

This example shows the possibility of applying our assertions to the problems of chemical structures.

Mechanisms of Exchange Reactions

The reviewed assertions on the two types of hydrogen exchange may serve as a basis for further conclusions on its mechanism.

1. The exchange of the first type through type (A) does not require a large activation energy. In the analogous mechanism of electro-conductivity of Grottus it equals 2-3 kcal/mole. However, in the case of proton transfer along a chain steric conditions are more favorable. We do not have any experimental data on the activation energy required in the exchange of the fast type, but judging by its rate, it is permissible to place it at not more than 8-10 kcal/mole. The entropy of activation in an exchange of this type is also large because of partial alignment of the hydrogen bonds. Under these conditions the exchange is always very fast.

2. As shown earlier (2), contrary to popular belief, an exchange of this type is effected by a molecular and not by an ionization mechanism. Electrolytic dissociation

should, as a rule, be a much slower process than an exchange through complex (A), since it is tied up with the breaking of at least one of the valence bonds:

$$(C) \quad \begin{array}{c} X\text{----}H \\ | \\ D\text{----}Y \end{array} \quad \longrightarrow \quad D:X:H^- + Y^-$$

The energy compensation in this process is effected not by internal complex transitions, as in the exchange of the fast type, but by the formation of solvent bonds with the molecules of the solvent*. Electrolytic dissociation, of course, also brings about hydrogen exchange, but it is a parallel, and, as a rule, slower way for it. The high rate of hydrogen exchange, even in negligibly small balanced concentrations of oxonium ions, also convinces us of the molecular mechanism of exchange in the fast type. These considerations evidently do not apply to exchange in strong electrolytes which are present in solution in the form of free (solvated) ions prior to the exchange.

The independence of the fast type exchange of electrolytic dissociation is confirmed by the already mentioned work of Kwart and associates, who found that the exchange $H_2O + D_2O$ and $CH_3OH + D_2O$ in vapors, where electrolytic dissociation is excluded, proceeds just as fast as in a liquid medium. In this connection we may note that the study of exchange in the gaseous phase under homogenous conditions, and at temperatures excluding resolution into radicals, was till now given little attention.

3. In the exchange of the slow type the activation energy is high, as a rule, and may change within wide limits depending on molecular structure, acidity of medium, etc.
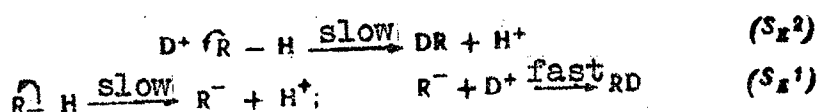
These, factors, which essentially determine the kinetics of the slow type exchange, play, as noted above, a secondary part in the fast type exchange**. Unlike the

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*The reviewed considerations are valid also when a larger number of molecules take part in the process, e. g., in the trimolecular mechanism (19), founded on the works of Swain (20), Ye. A. Shilov (21) and others.
**An exaggerated meaning is often given to the experimental study of activation energy. In most cases its value is found to be about 20-35 kcal/mole, irrespective of exchange materials, simply because these are the limits outside which exchanges are referred to as "immeasurably large" or "immeasurably small." Comparison of activation energies of exchange

latter, the slow type exchange may, and often does, proceed through electrolytic dissociation, if the activating energy of H and D transition in complex (B) is commensurate or smaller than that required for resolution into (C) ions. Depending on their relationship, the slow type exchange proceeds by the molecular (associative) or ionization mechanism. The presence or absence of electron pairs should be decisive not only for the kinetics, but also for the dynamic reaction of proton transfer. The very low acidity of hydrocarbons is well explained by the fact that the C-H bonds do not have free electron pairs, thus greatly handicapping transfer.

Kinetically both mechanisms of slow exchange correspond to Ingold's (22) mechanism S2 and S1 of displacement reactions which are distinguished by slow molecular steps, e. g., the electrophilic displacement of hydrogen:

$$D^+ \widehat{R} - H \xrightarrow{\text{slow}} DR + H^+ \qquad (S_E^2)$$

$$\widehat{R} H \xrightarrow{\text{slow}} R^- + H^+; \qquad R^- + D^+ \xrightarrow{\text{fast}} RD \qquad (S_E^1)$$

Molecular complex (B) corresponds to mechanism S2, while exchange with preliminary ionization corresponds to mechanism S1. A detailed study of the kinetics permits a determination on which of the two mechanisms this or the other reaction of displacement follows (23). For this we still do not have sufficient data on exchange reactions.

4. Classifying the mechanisms of hydrogen exchange into associative and ionic has sufficient basis. Although only the first is characteristic for exchange of the first type, both forms meet in the slow exchange. Depending on the rate of bond polarization in the transitory complex and the medium, there appear all kinds of transitory states of both mechanisms, and on this basis the pointlessness of such classification was indicated (3). We are unable to agree to this. Because of the rapid decrease of strength with increasing distance in covalent bonds their exchange proceeds more or less discretely as freely displacing ions are formed, thus permitting distinction with sufficient certainty between the polarizing complex and free ions. This distinction is as well founded as the division of chemical bonds into covalent and ionic bonds, irrespective of

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would be useful only in the study of monotype systems, or the study of kinetics beyond the indicated limits.

the fact that in actual molecules we find only transitory forms between them.

It is possible to show concrete experimental results which differentiate the two mechanisms of exchange. One of these, based on determining molecularity at slow rate from kinetic data, was cited above. Another refers to localizing the points of separation and combination of the proton and deuteron. In case of associative exchange the separation and combination in the intermediary complex proceeds most easily in the same bond. It is not necessarily so in the ionization mechanism and the exchange (carbonyl compounds, for example) is often accompanied by a transfer of the reaction center, with the result that the deuteron becomes attached to another atom, not the one from which the proton was detached. Without such a transfer of reaction center the kinetic regularity found in such exchanges as racemization, enolization, and halogenation of ketones would be incomprehensible.

5. In the ionization mechanism the first step of exchange may be presented by schemes:

$$\text{or} \qquad \overline{XH} + \dot{Y}D \longrightarrow X^- + HYD$$

$$\overline{XH} + YD \longrightarrow DXH + Y^-$$
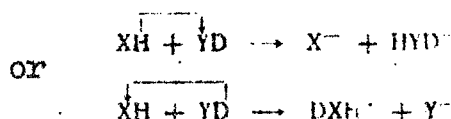
depending on the acidity relations of XH and YD. This same scheme responds to acid-base catalysis, if YD is the catalyst in equilibrium exchange with the solvent – donor of deuterium.

However, in the C-H bond exchanges of organic compounds there are no free electron pairs around the carbon atom and the equivalence of both schemes is destroyed. A proton may split away from a C-H bond more or less easily, but its attachement to a tetravalent carbon is always difficult, and to understand this requires additional suppositions, such as the formation of π-complex, or preliminary ionization.

In a basic medium a hydrocarbon may give off a proton from a C-H bond through ionization (D), as well as through a complex of the type (E):

$$\bar{C} - \overset{+}{H} \longrightarrow \bar{Y}$$
$$(D)$$

i. e., the exchange may proceed through ionization as well

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as through the associative molecular mechanism. Thereby, in a moderately basic medium, because of the low nucleophilic character of carbon in the C-H bond scheme (D) seems most advantageous. In such a complex the exchange follows more easily than by the formation of free ions, where the carbon would have to function as a base. Therefore, as shown by Ingold (24) earlier, in an acid medium, or in the presence of acid catalysts, a typical exchange proceeds by the ionization mechanism.

Of course these are only general rules from which individual cases of highly active groups, or secondary chemical processes may form exceptions.

6. If one is to except a trivial case of ion exchange with ionization mechanism, such as for example between KOH and D_2O, then exchange by nuclear displacement in C-H bonds requires the formation of intermediary complex (F)

$$\overset{+}{C}\diamondsuit\overset{H}{\underset{D}{\diamondsuit}}\overset{+}{Y} \quad or \quad C-H \longrightarrow \overset{+}{C}+H^- \\ (F) \qquad\qquad (G)$$
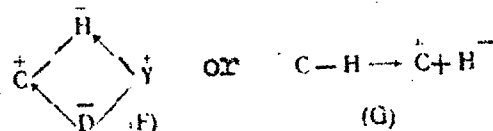
or the transfer of the free hydride ion (G). Energetically, exchange by complex (F) seems to be unprofitable because of the low electrophilic nature of carbon in C-H bonds, and there is no experimental data pointing in that direction. The transfer of the hydride is the generally accepted mechanism of a series of reactions in concentrated bases, e.g., the basic melting of phenols, a method often cited in the recent literature to explain other reactions. However, there is still no data that would justify considering this mechanism as one of the common ways of exchange. Moreover, as shown by G. P. Miklukhin (25), the transfer of the hydride ion in such media as water or alcohol is hardly probable as the H^- would immediately react with the medium giving H_2, which is not observed, and it would not bring about a hydrogen exchange.

These considerations strengthen the foregoing proposition that, as a rule, the exchange H-D takes place by the associative mechanism through the electrophilic complex (E), and not by way of nucleophilic substitution.

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